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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,790	12/05/2000	Mark H. Tuszynski	041673/2047	8867

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/730,790	TUSZYNSKI ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005 and 30 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,9,10 and 21-46* is/are pending in the application.

4a) Of the above claim(s) *6,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 21-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6-17-05 & 10-12-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments filed 10-12-05 and 12-30-05 have been entered. The declaration by Dr. Mark Tuszynski filed 10-12-05 has been entered. Claims 22, 30, 31 and 33 have been amended. Claims 1, 6, 9, 10 and 21-46 are pending. Claims 1 and 21-46 are under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and 33-46 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for improving motor function and neuronal density of Parkinson disease (PD) monkey model or Alzheimer's disease (AD) monkey model by injecting lentiviral vector encoding GDNF and NGF, respectively, into preselected brain regions of said monkey as discussed in the declaration by Dr. Mark Tuzynski, does not reasonably provide enablement for a method for ameliorating neuronal atrophy and loss in a mammalian brain by delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of neurotrophin at, or within diffusion distance of, targeted neurons to stimulate non-chemotropic growth in the targeted neurons, or a method for stimulating neuronal growth and activity by delivering a neurotrophin-encoding transgene composition via various administration routes to a region of the brain having targeted neurons and the expressed growth factor stimulates growth of neurons in **another region** of the brain. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 4-14-05. Applicant's arguments filed 10-12-05 and 12-30-05 have been fully considered but they are not persuasive.

Applicants cite references Conner, Curtis, von Bartheld, 2001, and von Bartheld, 1996, and argue that it was known in the art that growth factors have the ability of retrograde or anterograde transport within the neurons, therefore, one of ordinary skill in the art would appreciate that a neurotrophin expressed in, or taken up by, a neuron at one site may exert influence over growth of the neuron at a significant distance from that site (amendment, p. 16). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-14-05. The claims encompass various types of neurons in the brain, such as motor neurons, bipolar neurons, Golgi type I and type II neurons, multipolar neurons, nonadrenergic, noncholinergic neurons etc., wherein delivery of a neurotrophin-encoding transgene composition via various administration routes to a region of a targeted neuron would stimulate growth by, or activity in, said neuron in another region of the brain innervated thereby. The specification fails to provide adequate guidance and evidence for how to deliver a neurotrophin-encoding transgene composition to a region of a mammalian brain having targeted neurons via various administration routes such that expression of said neurotrophin at the delivery site would stimulate neuronal growth and activity in neurons in any other region innervated thereby in said mammalian brain. The declaration by Dr. Tuzynski only discloses improving motor function and neuronal density of Parkinson disease (PD) monkey model or Alzheimer's disease (AD) monkey model by injecting lentiviral vector encoding GDNF and NGF, respectively, into

preselected brain regions of said monkey. PD is associated with dopaminergic neurons and AD is associated with cholinergic neurons. The disclosure by Dr. Tuzynski's declaration fails to enable the full scope of the claimed invention. Further, the declaration fails to demonstrate that the improvements of motor function and neuronal density in monkey model are due to the non-chemotropic action of the expressed neurotrophin encoded by the administered lentiviral vector.

Applicants cite Example IV of the instant invention, US Patent No. 6,815,431 (10/032,952 **NOT 09/730,790**), and Dr. Tuzynski's declaration and argue that in vivo delivery of a growth factor expressing vector into the forbrain and striatum influenced activity and growth in the cortex and substantia nigra, respectively, and improvement in motor function and cognition in PD and AD animal models. Applicants further argue that in human clinical trials, expression of exogenous neurotrophin slows down the progression of AD in a patient by 51% (amendment, p. 17-19). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-14-05 and the reasons set forth above. It should be noted that the Application No. for US 6,815,431 is 10/032,952 NOT 09/730,790, and Example IV of the instant invention does not disclose in vivo delivery of growth factor expression vector into brain rather it discusses AchE staining pattern in the brain of cell-grafted animals. As discussed above, the declaration by Dr. Tuzynski only discloses improving motor function and neuronal density of Parkinson disease (PD) monkey model or Alzheimer's disease (AD) monkey model by injecting lentiviral vector encoding GDNF and NGF, respectively, into preselected brain regions of said monkey. PD is associated with dopaminergic neurons and AD is associated with cholinergic neurons. The disclosure by Dr. Tuzynski's declaration fails to enable the full scope of the claimed invention. Further, the declaration fails to demonstrate that the improvements of motor function and

neuronal density in monkey model are due to the non-chemotropic action of the expressed neurotrophin encoded by the administered lentiviral vector. US Patent No. 6,815,431 only discloses anterograde transport of GDNF expression product from striatum to substantia nigra but fail to demonstrate amelioration of neuronal atrophy or stimulation of neuronal growth and activity in innervated neurons that are distant from neurons expressing a neurotrophin protein via non-chemotropic action of said neurotrophin protein. Thus, claims 1 and 33-46 remain rejected under 35 U.S.C. 112 first paragraph.

3. Claims 1 and 21-32 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for improving motor function and neuronal density of Parkinson disease (PD) monkey model or Alzheimer's disease (AD) monkey model by injecting lentiviral vector encoding GDNF and NGF, respectively, into preselected brain regions of said monkey as discussed in the declaration by Dr. Mark Tuzynski, does not reasonably provide enablement for a method for ameliorating neuronal atrophy and loss in a mammalian brain by delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of neurotrophin at, or within diffusion distance of, targeted neurons to stimulate non-chemotropic growth in the targeted neurons, i.e. dopaminergic neurons and cholinergic neurons. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 4-14-05. Applicant's arguments filed 10-12-05 and 12-30-05 have been fully considered but they are not persuasive.

Applicants cite Example IV of the instant invention, US Patent No. 6,815,431 (10/032,952 **NOT 09/730,790**), and Dr. Tuzynski's declaration and argue that in vivo delivery of a growth factor expressing vector into the forbrain and striatum influenced activity and growth in the cortex and substantia nigra, respectively, and improvement in motor function and cognition in PD and AD animal models. Applicants further argue that in human clinical trials, expression of exogenous neurotrophin slows down the progression of AD in a patient by 51% (amendment, p. 17-19). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 4-14-05 and the reasons set forth above. It should be noted that the Application No. for US 6,815,431 is 10/032,952 **NOT 09/730,790**, which is instant invention, and Example IV of the instant invention does not disclose in vivo delivery of growth factor expression vector into brain rather it discusses AchE staining pattern in the brain of **cell-grafted animals**. As discussed above, the declaration by Dr. Tuzynski only discloses improving motor function and neuronal density of Parkinson disease (PD) monkey model or Alzheimer's disease (AD) monkey model by injecting lentiviral vector encoding GDNF and NGF, respectively, into preselected brain regions of said monkey. The disclosure by Dr. Tuzynski's declaration fails to demonstrate that the improvements of motor function and neuronal density in monkey model are due to the non-chemotropic action of the expressed neurotrophin encoded by the administered lentiviral vector. US Patent No. 6,815,431 only discloses anterograde transport of GDNF expression product from striatum to substantia nigra but fail to demonstrate amelioration of neuronal atrophy or stimulation of neuronal growth and activity in innervated neurons that are distant from neurons expressing a neurotrophin protein via non-chemotropic action of said neurotrophin protein. Anterograde or retrograde transport of expressed neurotrophin protein within brain does

not mean that sufficient amount of the expressed neurotrophin protein would be present in distant innervated neurons such that amelioration of neuronal atrophy or stimulation of neuronal growth and activity in said innervated neurons would be obtained in vivo. The human clinical trial data fails to demonstrate that the slowing down of AD progression in human patient is due to the non-chemotropic action of the expressed exogenous neurotrophin, or such data is just the effect of the expressed neurotrophin in the target neurons at the delivery sites. Thus, claims 1 and 21-32 remain rejected under 35 U.S.C. 112 first paragraph.

Conclusion

No claim is allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER